



## Correspondence

## Can influenza vaccine modify COVID-19 clinical course?

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## Dear Editor,

With the continued COVID-19 pandemic and the fear of a second wave, the world in the Northern hemisphere is facing the occurrence of COVID-19 and influenza with the upcoming winter season. Currently, there are limited therapeutic options and no available vaccine. Heterotypic immunity (cross-protection) is the protection of some individuals to subtypes of influenza virus to which they have not previously been exposed through natural infection or immunization. A possible explanation has arisen from an understanding of the molecular targets of broadly neutralizing monoclonal antibodies directed against various portions of the hemagglutinin (HA) protein. A specific region of the HA stem is highly conserved among many influenza strains, and it has been possible to stimulate the production of stem-targeting antibodies with cross-neutralizing properties in several host species, including non-human primates. Immune responses to the 2009 H1N1 pandemic included broadly cross-reactive antibodies against the HA stalk and head domain epitopes of multiple influenza strains. In the case of the 2009 H1N1 influenza vaccine, the majority of HA-specific antibodies from healthy recipients had broad cross reactivity to the HA stem, and three broad cross-reactive antibodies were shown to bind the HA stem. The identification of predictive signatures of vaccines would allow the development of a vaccine chip with a few hundred genes that could interrogate a particular type of innate or adaptive immune response (e. g., magnitude of effector CD8 T-cell response; frequency of Th cells; balance of Th1, Th2, and Th17 cells; and high-affinity antibody titers). Such an approach would permit rapid identification (or prediction) of suboptimal responses in the elderly, infants and immunocompromised individuals.

Currently, there are no specific antiviral drugs or approved vaccines for SARS-CoV-2. Symptomatic treatment strategies are the recommendation in addition to enrollment of patients in clinical therapeutic trials. SARS-CoV-2 infects the lower respiratory tract and cause severe pneumonia and may lead to fatal acute lung injury and acute respiratory distress syndrome (ARDS). SARS-CoV-2 may develop ways to avoid early detection by the immune system. Once detected by the immune system, this immune response may result in intense response such as the cytokine storm and may aggressively destroy infected cells and results in

tissue and organ destruction.

It was found that of influenza vaccination was associated with lower risk of COVID-19 infection and influenza vaccination rate was 93.9% among 5940 of non-COVID-19 vs. 6.1% among 384 COVID-19 positive cases [1]. In addition, 10% increase in influenza vaccination coverage was associated with a statistically significant 28% reduction in COVID-19 death rate in the elderly [2]. In a pre-print study of 92,664 COVID-19 patients of which about one-third received influenza vaccine. Influenza vaccinated patients had 8% lower odds of intensive care unit admission, 18% lower odds of requiring mechanical ventilation and 17% lower odds of death [3]. It is possible that influenza vaccination could act as a non-specific immune stimulator in patients with COVID-19 leading to early activation of the immune system to attack SARS-CoV-2 before invading cells. Stimulation of the immune system by influenza vaccines could occur through early activation of the immune system by influenza vaccine which facilitate early detection of SARS-CoV-2. Influenza vaccine keeps the immune system active through Toll-Like Receptor 7 [1]. Toll-Like Receptor 7 is an important binding of single-stranded RNA respiratory viruses, such as SARS-CoV-2 [4]. Influenza A infection up-regulates pulmonary ACE2 receptors and thus leads to increased SARS-CoV-2 infection [5].

The most common seasonal influenza vaccine given to humans is the inactivated trivalent vaccine, which targets the three most representative virus types in circulation (two subtypes of influenza A and one influenza B virus). Live attenuated influenza vaccines (LAIVs) made of temperature-attenuated reassortant virus also come in both trivalent (two subtypes of influenza A viruses and one B virus) and quadrivalent (with an additional B virus) form. Inactivated influenza vaccines are injected intramuscularly, and LAIVs are administered intranasally. For inactivated influenza vaccines, an HA inhibition titer of 1:40 has been established as an immunologic correlate of 50% protection in adults children require 1:110 to achieve 50% protection [6]. In a risk analysis study, the infection risk of SARS-CoV-2 was reduced in those who had pneumococcal polysaccharide or influenza vaccine [1]. In addition, live attenuated vaccines stimulate the innate immunity and provide transient protection against COVID-19 as SARS-CoV-2 infection was associated with suppression of the innate immunity. Thus, it seems prudent than before that we continue to promote influenza vaccines in this

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season. Further studies are needed to further delineate the role of influenza vaccines in modifying the course of SARS-CoV-2 infection.

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## Declaration of competing interest

All authors have no conflict of interest to declare.

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